

REMARKS

Applicant respectfully requests reconsideration. Claims 1, 2, 4, 5, 9-11, 42-49 and 51-55 were previously pending in this application. Claims 10 and 51 were withdrawn. As a result, claims 1, 2, 4, 5, 9, 11, 42-49 and 52-55 are pending for examination. No new matter has been added.

Interview Request

Applicant respectfully requests a telephone interview with the Examiner in the event that this amendment does not place all claims in condition for allowance.

Rejection Under 35 U.S.C. § 112, First Paragraph

The Examiner maintained the rejection of claims 1, 2, 4, 5, 9, 11, 42-50 and 52-55 under 35 U.S.C. § 112, First Paragraph, as allegedly lacking enablement. Applicant notes that claim 50 was canceled in the Amendment filed on Sept. 14, 2007, so believes that rejection of this claim is moot.

Applicant respectfully traverses the rejection. The Examiner's assertions for why the claimed invention lacks enablement rest on the question of predictability of expression levels of MAGE-10 in cancer. The Examiner states, "One cannot predict that the antibodies produced by the claimed peptides could be used for detecting cancer, because one cannot predict that the protein MAGE-10 (SEQ ID NO:1) is overexpressed in cancer in sufficient quantity such that it could be detected by its antibodies." Thus the Examiner concludes that Applicant has not taught one of ordinary skill in the art how to use the claimed polypeptides of the invention.

Applicant includes herein an article by Huang et al., "Cytolytic T lymphocytes recognize an antigen encoded by MAGE-A10 on a human melanoma," *J. Immunol.* 1999, 162:6849-6854. The lead author on this paper is also the first-named inventor on the instant application. In this reference, Huang et al. clarifies the issue of expression levels of *MAGE-A10*. On page 6851 of the article, Huang et al. states,

"In a previous report, we suggested, on the basis of semiquantitative RT-PCR assays, that all the tumors expressing *MAGE-A10* expressed the gene at a very low level (4). The level we observed was deemed unlikely to be sufficient for the production of enough antigenic peptides to allow recognition by CTL (38). However, it was later observed with a mAb that a tumor with a high level of

MAGE-A1 expression contained similar amount of *MAGE-A1* and *MAGE-A10* protein (39). This led us to reconsider our *MAGE-A10* assay, and we have now reached by two different methods the conclusion that the tumors expressing *MAGE-A10* express this gene at levels that are similar to those observed for *MAGE-A1*...we conclude that there is no discrepancy between the level of expression of *MAGE-A10* and the fact that an Ag [antigen] encoded by *MAGE-A10* can be recognized by a CTL."

Thus the Huang et al. article reveals that *MAGE-A10* is expressed at higher levels in cancer than previously thought, and at comparable levels to *MAGE-A1*, indicating a predictability of expression levels of *MAGE-A10* in cancer. Moreover, both the instant specification and Huang et al. show that *MAGE-A10* is expressed in a broad range of cancer types.

Applicant also includes herein an article by Valmori et al., "Frequent cytolytic T-cell responses to peptide *MAGE-A10*₂₅₄₋₂₆₂ in melanoma," *Cancer Res.* 2001, 61:509-512. Fig. 2B in this reference presents a Western blot indicating expression of *MAGE-A10* in melanoma cells, and on page 511 (left column) the article states, "peptide *MAGE-A10*₂₅₄₋₂₆₂ appears to be among the most immunogenic melanoma-associated antigens described thus far."

Applicant asserts that both of the references included herein emphasize the predictability of expression and immunogenicity of *MAGE-A10* peptides.

The Examiner further asserts that there is no indication that the CTL cell line CTL447A/5, discussed in the specification, would recognize and lyse any primary cancer cells. While Applicant is not aware of any lysis experiments that are routinely performed with pure tumor tissue, Applicant notes that the cell line used in these experiments (LB1751-MEL) is a primary young cell line and therefore is as close to pure tumor cells as possible. Furthermore, Applicant asserts that one of ordinary skill in the art would recognize that CTL binding is analogous to antigen binding and recognition.

Applicant has taught how to make and use the claimed invention. The teachings of the specification permit one of ordinary skill in the art to practice the claimed isolated polypeptides and nonapeptides of defined sequence. The teachings of the specification are confirmed by the report of Huang et al. in *J. Immunol.* provided herewith regarding increased *MAGE-A10* expression in cancer as determined using improved assays. More specifically, Huang et al.

concludes that the level of expression of *MAGE-A10* is sufficient to provide antigen that can be recognized by CTLs.

Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection of the claims under 35 U.S.C. § 112, First Paragraph.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,

/John R. Van Amsterdam/
John R. Van Amsterdam
Reg. No. 40,212
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210
Telephone: (617) 646-8000

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